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ODOR AND IRRITATION EFFECTS OF A VOLATILE ORGANIC COMPOUND MIXTURE

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Human exposure to volatile organic compounds elicits a variety of symptoms, many of which are thought to be mediated by the olfactory and trigeminal systems. This report describes evidence indicating that perceived odor intensity diminishes during prolonged exposure, whereas irritation of the eyes and throat reaches an asymptotic level. Both odor and irritation apparently influence the assessment of air quality.

INTRODUCTION

Exposure to pollutants commonly found in nonindustrial indoor air became an international health concern during the past decade (13). One class of pollutants commonly found in the indoor environment is volatile organic compounds (VOCs). More than three hundred VOCs have been identified in indoor air (4,15). The chief sources of these contaminants are building materials, combustion processes and consumer (cleaning, personal care) products. Although objective indicators of adverse health effects resulting from exposure to low-level mixtures of VOCs remain illusive, a set of symptoms which characterize the "sick building syndrome" (SBS) has been defined (16). The symptoms, often reported by occupants of new or recently renovated buildings, include irritated eyes, nose and throat, headache, mental fatigue and respiratory distress.

Effects of exposure on subjective reactions have been investigated by exposing healthy humans to a mixture of VOCs in an experimental chamber (12). The highest exposure level was 25 mg/m³ of the twenty-two VOCs found most commonly or at highest concentrations in a sampling of new Danish homes, excluding known carcinogens (13). Results from a questionnaire indicated that subjects perceived significantly degraded air quality, increased odor intensity, altered skin temperature and reduced ability to concentrate during exposure, relative to clean air. Subjects also adjusted a potentiometer over the course of the 2.75 hr test period to indicate the perceived intensity of combined eye, nose and throat irritation. Irritation increased significantly during exposure, showing an initial rapid increase with little or no evidence of a decline, or adaptation, by the end of exposure. The results suggested that both the olfactory (odor) and trigeminal (irritation) systems may have contributed to the subjects' perceptions.

Concerns have been expressed that irritation and other symptoms of SBS may simply reflect a psychosomatic response to detection of an aversive odor, similar to explanations proposed for the "chemical hypersensitivity syndrome"

(reviewed in 2,3). Evidence differentiating responses mediated by the olfactory and trigeminal nerves would argue against the psychosomatic hypothesis. For example, if perceived odor intensity declined during exposure, but perceived irritation intensity increased or reached asymptotic level, irritation level could not be a simple function of odor intensity. Characterization of the time course of odor and irritation intensity during VOC exposure, therefore, might lend insight to the contributions of the olfactory and trigeminal systems to the symptoms of SBS. The current experiment was conducted on sixty-six adult males in a controlled chamber environment. All subjects participated in a clean air session and a session with exposure to VOCs similar to the mixture used by Molhave et al. (12).

METHODS

Subjects

Sixty-six healthy Caucasian male subjects ranging in age from 18-39 yrs (mean=25.0, SD=5.6) participated in the experiment. Prospective subjects were screened for physical and psychological abnormalities with questionnaires, physical examinations, allergy tests and the MMPI. Healthy, nonsmoker candidates were accepted as subjects.

Procedures

All subjects participated in training, clean air and exposure sessions, separated by intervals of at least one week. The order in which experimental conditions were assigned was counterbalanced, and neither the experimenter conducting the sessions nor the subjects were informed of the order. Subjects practiced each of the tests under clean air conditions in a training session. Experimental sessions were 4 hrs in duration. The chamber always contained clean air for the first 75 min, during which baseline measurements were obtained. VOC concentration in the chamber was brought to target level (0 or 25 mg/m³) during the next 30 min (buildup period). Exposure level remained constant (+3%) for the remaining 2.25 hrs. The mixture of twenty-two VOCs was identical to that used by Molhave et al. (12) with the exception that 1,1 dichloroethane was substituted for 1,2 dichloroethane.

Measurements

Potentiometer. Subjects indicated the intensity of combined eye, nose and throat irritation by adjusting a sliding bar along a low-to-high scale, as was done in the Molhave et al. (12) study. Ratings were obtained using a linear potentiometer which subjects were asked to adjust whenever they felt a change in sensation level, as well as at intervals of 15-30 min. Potentiometric ratings were sampled at 15 min intervals. Calibration measurements were used to formulate a translation of the data points to a 0.0-4.0 scale.

Questionnaire. A computerized questionnaire of 25 items (12) was presented on a video screen to subjects during the baseline period, immediately after the buildup period and shortly before the end of the session. The first three questions required "yes" or "no" answers. A horizontal line appeared below each of the other twenty-two question, and both ends of the line were labelled with an extreme such as "not at all" and "very much". Subjects indicated the intensity of their perceptions by positioning a cursor along the line using a joy stick. Cursor position was translated to a scale ranging from 0-30.

Analyses

Response profiles were constructed for both air and VOC sessions by calculating means and standard deviations at each sampling point. This

resulted in three pairs (clean air and VOC) of data points for each item in the questionnaire and 17 pairs for the potentiometric data. Each pair of response profiles was tested for parallelism using a multivariate analysis of variance of repeated measures method. Significance level was set at probability = 0.05. If the parallelism hypothesis for a question was rejected, group differences at mid-exposure, post-exposure and mid- to post-exposure were tested for significance with two-way analyses of variance.

RESULTS

Potentiometer

Group-average estimations of combined eye, nose and throat irritation intensity are displayed across time for both clean air and VOC sessions in Figure 1. In the VOC sessions, perceived irritation began to increase sharply at the onset of exposure (75 min), and peaked at 150 min. Irritation level remained roughly constant throughout the remainder of the session. The magnitude of perceived irritation gradually increased throughout the course of the clean air sessions. The difference between air and VOC response functions was statistically significant ($F(16,47)=3.98$, $p<0.001$).

Questionnaire

Group-average ratings for twenty-two questions, collected during the baseline period (pre), just after the buildup period (mid) and shortly before the end of the exposure period (post), were calculated for both clean air and VOC sessions. Significant effects were found for six items: odor intensity ($F(1,65)=77.9$, $p<0.001$), eye ($F(1,65)=4.13$, $p=.021$) and throat ($F(1,65)=4.41$, $p=.016$) irritation, headache ($F(1,65)=9.52$, $p<0.001$), drowsiness ($F(1,65)=4.38$, $p=.017$) and air quality ($F(1,65)=32.86$, $p<0.001$). Perception of five environmental variables which were held constant (light and noise levels, room temperature, humidity and air movement) and eleven other variables (nose, face and body skin irritation, face and body temperature, eye, face and body skin moisture, sluggishness, coughing and concentration) were not significantly affected by exposure.

Means of the six significant variables are displayed in Figure 2. Note that the perceived magnitudes of eye and throat irritation, headache and drowsiness showed no evidence of adaptation, or a decrease between mid and post scores. In contrast, perceived odor intensity decreased by 30% between the mid and post scores, relative to the baseline score. This decrease in odor intensity between mid and post scores for VOC sessions relative to clean air sessions was significant ($F(1,65)=12.79$, $p<0.001$). Also, a smaller (18%) but significant decrease in dissatisfaction with air quality was seen by the end of exposure ($F(1,65)=5.30$, $p<0.024$).

All three of the yes/no questions showed significant differences between clean air and VOC sessions. The question on whether or not staying in the chamber is comfortable showed a lower percentage of "yes" responses for the VOC sessions in both mid and post scores ($F(1,65)=15.19$, $p<0.001$), but the difference between the mid and post scores was not significant. The question on satisfaction with this level of air quality in the home environment also differed significantly between groups in both the mid and post scores ($F(1,65)=44.68$, $p<0.001$). Dissatisfaction was greater at the mid score than at the post score ($F(1,65)=4.84$, $p<0.031$). The question on whether or not subjects would ventilate their home more if air quality was like that in the chamber also differed significantly between groups at the last two measurement

time points ($F(1,65)=22.35$, $p<.001$), but the difference between mid and post scores was not significant.

DISCUSSION

The results reported by Molhave et al. (12) on potentiometric ratings of the magnitude of combined eye, nose and throat irritation were confirmed in the current study. Perceived irritation increased significantly more during 2.75 hrs of exposure to VOCs than during clean air sessions. Irritation magnitude reached an asymptotic level after about 75 min of exposure. This result was supported by eye and throat irritation ratings in questionnaire data collected before, during and near the end of exposure. The questionnaire data also indicated that nose irritation was greater during VOC sessions than clean air sessions, but this result did not reach significance. None of these variables showed any adaptation, or decrease between mid and post scores. On the other hand, ratings of odor intensity did show evidence of adaptation. Perceived odor intensity rose sharply between pre and mid scores and then declined by an average of 30% in the post score. The time-course functions for irritation and odor thus distinguished responses thought to be mediated by the trigeminal and olfactory nerves, respectively. Irritation levels increased or remained constant as perceived odor intensity decreased over time, indicating that complaints of irritation are not a simple function of odor intensity.

Significant effects also were seen in ratings of headache, drowsiness and air quality. Time course functions for headache and drowsiness were similar to those for irritation in that no decrease was seen between mid and post scores. However, dissatisfaction with air quality declined between mid and post scores by roughly one half the percentage seen with odor intensity. These results suggest that both irritation level and odor intensity may contribute to the perception of air quality. This hypothesis is consistent with results from the yes/no questions in which a significantly greater percentage of subjects indicated that the level of air quality in the chamber would be acceptable in their home environment at the post score than at the mid score.

Although VOCs apparently stimulate both trigeminal and olfactory receptors, activity in these systems is probably not independent of each other. Studies have shown that the addition of an odorant to an irritant reduces perceived irritation intensity (10). Conversely, the addition of an irritant to an odorant reduces perceived odor intensity (9). Two factors may account for the observation that odor magnitude showed adaptation of only 30%, whereas adaptation often reaches a level of 50-70% (5). First, some adaptation may have occurred during the buildup period, thereby reducing odor magnitude at the mid score relative to what it would have been if subjects had entered the chamber with VOC concentration at the target level. Second, the irritation quality of the VOC mixture probably caused a reduction in odor adaptation. Adaptation level for n-butylacetate after 3 hrs of exposure is about 60% at a concentration of 0.75 mg/L, but is only about 50% at a concentration of 18.6 mg/L (5). Since irritation-concentration growth functions are typically much steeper than odor intensity-concentration functions (11 from 7,8), this reduction in adaptation was attributed to a greater proportion of irritant to odorant quality at the higher concentration.

Irritation intensity can exhibit both adaptation and potentiation, or growth over time, under some conditions (10). Four factors may account for the current result that irritation intensity did not show adaptation. First, at low concentrations, irritation intensity generally shows potentiation, but not

adaptation (8,10). Second, when subjects are in the chamber during the buildup period, potentiation is seen for longer periods of time than if subjects enter the chamber with concentration at a steady-state level (1,10). Third, the latency for perceiving maximal irritancy is greater than that for perceiving maximal odor intensity (6). The free nerve endings of the trigeminal nerve are more deeply embedded in the nasal mucosa than the cilia of olfactory receptors. Stimuli may reach the trigeminal receptors in slowly increasing concentrations before reaching a steady-state level (8). Fourth, since perceived irritation increases as perceived odor decreases (10), irritation intensity would be expected to increase as odor adaptation occurred.

In conclusion, the current study suggested that both the olfactory and trigeminal systems were activated by the VOC mixture. Although the study looked at only three points in the time course of odor intensity, the evidence clearly indicated that perception of odor intensity decayed over time. Perceived intensity of irritation, on the other hand, showed no evidence of decay. Both odor and irritation apparently contributed to the perception of air quality.

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GROUP AVERAGE QUESTIONNAIRE DATA

GROUP-AVERAGE POTENTIOMETRIC DATA COMBINED EYE, NOSE AND THROAT IRRITATION

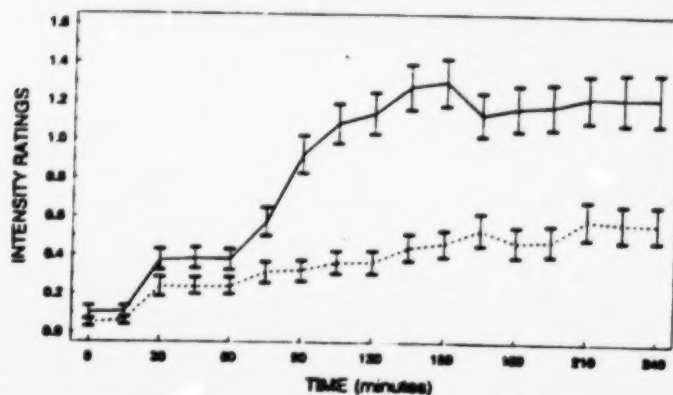


Fig.1

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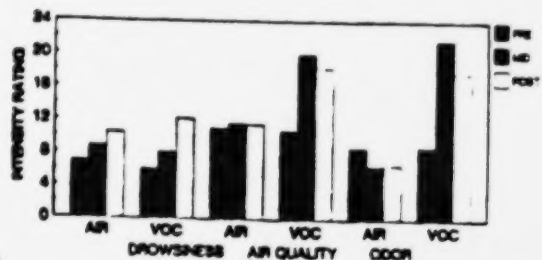
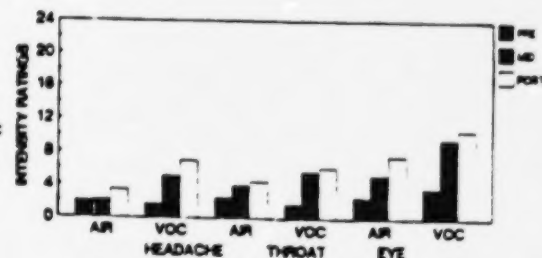


Fig.2